Application Number 10/772,537
Art Unit 1639

In the Specification:

Pursuant to Examiner's objection to the Specification as containing improper amino acid identifications according to the Sequence rules, please replace the following paragraphs:

Please replace the 1st full paragraph on page 4 that begins at line 15 as follows:

The purpose of this invention is to characterize the specific peptide fragment derived from specially prepared zinc charged fetuin wherein the fragment was found to contain an apoptosis-inducing activity. Specifically, the amino acid sequence of this peptide is ~~H-T-F-S-G-V-A-S-V-E (His Thr Phe Ser Gly Val Ala Ser Val Glu, SEQ ID NO: 1)~~ His Thr Phe Ser Gly Val Ala Ser Val Glu (SEQ ID NO: 1) and correlates to amino acid no. 300-309 of fetuin, referred to herein as Fetuin Peptide Fragment (FPF 300-09). FPF 300-09 strongly induced apoptosis in LNCaP (prostate cancer) and HT-29 (colon cancer) cells without affecting CCD 18 Co (normal colon) cells. The in vitro tissue culture study demonstrated that the FPF 300-09 is more potent than the parent molecule in inducing apoptosis. FPF 300-09 has a LD_{50} of 0.3-0.4 μM, while the LD_{50} for zinc-charged fetuin is 3-10 μM.

Further, please replace the 1st full paragraph on page 40 that begins at line 2 as follows:

The dried and reconstituted filtrate was found to contain peptide fragments. The amino acid sequence analysis revealed two major peptide fragments in the filtrate:

PAGE 4/59 * RCVD AT 5/5/2005 9:05:43 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-1/0 * DNIS:8729306 * CSID:3107778348 * DURATION (mm-ss):27-54

~~(1) H T F S G V A S V E (amino acid no. 300-309; His Thr Phe Ser Gly Val Ala Ser Val Glu; SEQ ID NO: 1) and~~

~~(2) S A S G E A F H (amino acid no. 310-317; Ser Ala Ser Gly Glu Ala Phe His; SEQ ID NO: 2) of fetuin.~~

(1) His Thr Phe Ser Gly Val Ala Ser Val Glu (amino acid no. 300-309; SEQ ID NO: 1) and

(2) Ser Ala Ser Gly Glu Ala Phe His (amino acid no. 310-317; SEQ ID NO: 2 of fetuin.

Still further, please replace the 2nd paragraph on page 40 that begins at line 9 as follows:

To identify which of these peptide fragments are responsible for the apoptosis-inducing activity, the two fragments ~~(H T F S G V A S V E~~ His Thr Phe Ser Gly Val Ala Ser Val Glu (amino acid no. 300-309; referred to herein as Fetuin Peptide Fragment (FPF 300-09); SEQ ID NO: 1) and ~~S A S G E A F H~~ Ser Ala Ser Gly Glu Ala Phe His (amino acid no. 310-317; SEQ ID NO: 2) of the full-length fetuin ~~molecule)~~ molecule were chemically synthesized. Upon in vitro testing of these chemically synthesized peptide fragments, FPF 300-09 was shown to have the greater apoptotic activity. LNCaP (prostate cancer cells) were incubated with FPF 300-09. In Fig. 10, chemically synthesized FPF 300-09 caused membrane "bubbling" in LNCaP cells after three (3) hours of incubation. Incubation of the peptide fragment (amino acid no. 310-317) or the peptide fragment (amino acid no. 300-307) with LNCaP cells did not show any apoptotic activity or membrane "bubbling." Fig. 9 shows the control of LNCaP cells without FPF

PAGE 5/59 * RCVD AT 5/5/2005 9:05:43 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-1/0 * DNIS:8729306 * CSID:3107778348 * DURATION (mm-ss):27-54

300-09. These results suggest that the peptide fragment that induced apoptosis and that was present in the filtrate corresponds to amino acid no. 300-309 of the full-length fetuin.

Yet further, please replace last paragraph on page 42 that begins at line 25 and that ends on page 43 at line 17 as follows:

In addition, peptide sequences were determined from other animal sera, including pig, sheep and mice. K.M. Dziegielewska, et al., Fetuin, 16-17, (R.G. Landes Co. 1995). These peptide sequences have a similarity of 60-90% with the fetuin isolated from bovine serum. The present application instructs that these similar fetuin peptide sequences will also have valuable apoptotic activity. The peptide sequences for FPF 300-09 for other species are:

Human (~~H T F M G V V S L G~~ His Thr Phe Met Gly Val Val Ser Leu Gly; SEQ ID NO: 3);

Pig (~~H S F S G V A S V E~~ His Ser Phe Ser Gly Val Ala Ser Val Glu; SEQ ID NO: 4);

Sheep (~~H T F S G V A S V E~~ His Thr Phe Ser Gly Val Ala Ser Val Glu; SEQ ID NO: 5);

Rat (~~H T F S G V A S V E~~ His Thr Phe Ser Gly Val Ala Ser Val Glu; SEQ ID NO: 6); and

Mouse (~~H A F S P V A S V E~~ His Ala Phe Ser Pro Val Ala Ser Val Glu; SEQ ID NO: 7). Id.

These analogs are also claimed as being taught by the current application.

PAGE 6/59 * RCVD AT 5/5/2005 9:05:43 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-1/0 * DNIS:8729306 * CSID:3107778348 * DURATION (mm-ss):27-54